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SUMMARY: The relative importance of the effect of outdoor environmental factors (suspended particulates, sulphur dioxide) and indoor environmental factors (parental smoking, gas cooking), on the respiratory health of children is still unclear. To answer these questions, a 3-yr cohort analytic study has been conducted in Hamilton, Ontario between 1978 and 1981. The prevalence of respiratory symptoms and indoor environmental factors was determined by an interviewer-administered questionnaire. Pulmonary function measures included both the forced expiratory maneuver and the single- and multiple-breath nitrogen washouts. Outdoor air quality was measured by a comprehensive network of suspended particulate and sulphur dioxide monitors. There were 3,345 children 7 to 10 yr of age studied in the first year, a response rate of 95.4%, 3,727 in the second year, and 3,168 in the third year; 75.6% of the initial cohort were studied in both Year 2 and Year 3. Comprehensive quality control in the study included measurement of the repeatability of both the questionnaire and pulmonary function data. Repeatability was acceptable except for variables derived from the single-breath nitrogen washout (correlation between initial and repeat closing volume vital capacity was 0.14). Cigarette smoking in Year 3 was reported in 4.8% of the children. The distribution of other covariables was not uniform, and the prevalence of parental smoking and gas cooking was greatest in the industrial area with the highest particulate pollution. Future analysis of these data will require the effect of these covariables to be distinguished from that caused by outdoor air pollution.

# A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children in Hamilton, Ontario

## Epidemiologic Survey Design, Methods, and Description of Cohort[1-3]

ANTHONY T. KERIGAN, CHARLES H. GOLDSMITH, and L. DAVID PENGELLY

**SUMMARY** The relative importance of the effect of outdoor environmental factors (suspended particulates, sulphur dioxide) and indoor environmental factors (parental smoking, gas cooking), on the respiratory health of children is still unclear. To answer these questions, a 3-yr cohort analytic study has been conducted in Hamilton, Ontario between 1978 and 1981. The prevalence of respiratory symptoms and indoor environmental factors was determined by an interviewer-administered questionnaire. Pulmonary function measures included both the forced expiratory maneuver and the single- and multiple-breath nitrogen washouts. Outdoor air quality was measured by a comprehensive network of suspended particulate and sulphur dioxide monitors. There were 3,345 children 7 to 10 yr of age studied in the first year, a response rate of 95.4%, 3,727 in the second year, and 3,168 in the third year; 75.8% of the initial cohort were studied in both Year 2 and Year 3. Comprehensive quality control in the study included measurement of the repeatability of both the questionnaire and pulmonary function data. Repeatability was acceptable except for variables derived from the single-breath nitrogen washout (correlation between initial and repeat closing volume vital capacity was 0.14). Cigarette smoking in Year 3 was reported in 4.8% of the children. The distribution of other covariables was not uniform, and the prevalence of parental smoking and gas cooking was greatest in the industrial area with the highest particulate pollution. Future analysis of these data will require the effect of these covariables to be distinguished from that caused by outdoor air pollution.

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### Introduction

The study of environmental factors responsible for respiratory disease in children is important for 2 reasons: (*1*) the absence of confounding factors, such as personal smoking and occupation, makes the interpretation of any observed association between air quality and respiratory disease more credible; and (*2*) the growing realization that respiratory illness during childhood may predispose to the development of respiratory morbidity and early mortality from respiratory illness during adult life (1, 2).

This particular usefulness of children has become more important as air quality has improved during the last decade (1970–1979) and levels become closer to the Ontario guidelines. For total suspended particulates (TSP), the Ontario objective (annual geometric mean) is 60 $\mu g/m^3$. In 1978, the annual TSP in Hamilton was 77 $\mu g/m^3$. For sulphur dioxide, the objective is 0.02 ppm annual average and the measured level was 0.016 ppm (3).

Studies in several countries from 1967 to 1978 have identified a number of environmental factors that might lead to respiratory disease in children. The initial study of the effect of the particulate/sulphur dioxide ($SO_2$) complex was conducted by Lunn and coworkers (4) and showed increased prevalence of respiratory symptoms and reduced pulmonary function in areas of poor air quality. Improvement in air quality led to a reduction in these adverse health effects (5). Follow-up studies in several towns in the United Kingdom by Melia and colleagues (6) showed that adverse health effects were now extremely difficult to find with the further improvement in air quality. These studies, however, did not consider the possible role of parental smoking.

As outdoor air quality improved, attention changed to indoor air quality, particularly in relation to parental smoking and indoor sources of gaseous pollutants such as gas stoves. The health effects from parental smoking appear to be most marked in the first years of life (7), but studies of this effect on older children have not yielded consistent results, some showing increased prevalence of symptoms (8) but others showing no effect (9, 10). Colley and coworkers (11) suggested that the effect of parental smoking may be due predominantly to the increased prevalence of parental cough. An effect of parental smoking on children's pulmonary function has also been shown (12, 13). The influence of gas cooking was first suggested by Melia and coworkers (14), although the effect seemed to decrease as the children became older. In contrast, Keller and colleagues (15) were not able to find any effect of gas cooking on children's respiratory symptoms.

The uncertainty about the role of low levels of TSP and $SO_2$, and their importance in relation to domestic environmental factors, led us in 1978 to initiate a 3-yr cohort study in Hamilton, Ontario that was designed to answer the following questions. (*1*) Is there an effect on children's respiratory health of suspended particulates and $SO_2$ at the present levels? (*2*) What is the effect of the various factors in the domestic environment when considered in relation to outdoor air quality?

The main study was preceded by a pi-

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TABLE 1

SUSPENDED PARTICULATE LEVELS BY AREA OF CITY (JANUARY THROUGH DECEMBER 1980)

| | WU | EU | WL | EL | IC |
|---|---|---|---|---|---|
| Total suspended particulates, $\mu g/m^3$* | 44 | 43 | 61 | 58 | 90 |
| TSP Load < 7.0 μ, % | 70.3 | 86.8 | 67.9 | 71.1 | 82.1 |
| Maximal daily average, $\mu g/m^3$† | 140 | 146 | 173 | 149 | 223 |
| Monitoring sites, n | 5 | 3 | 9 | 4 | 5 |

Definition of abbreviations: WU = west upper quadrant, EU = east upper quadrant, WL = west lower quadrant, EL = east lower quadrant, IC = industrial core

* Average of annual geometric means of all sites in each area.

† Average of daily maxima of all sites in each area.

lot study (16) which demonstrated that within Hamilton, Ontario, there existed substantial gradients across the city for suspended particulates and $SO_2$ that would enable us to study children with differing exposures in the same city. This offered major logistical advantages in a design similar to that of Lunn and coworkers (4). During the current study, these gradients for suspended particulates continued to be present. The levels in each area of the city during 1980 are shown in table 1 in terms both of the annual geometric mean and of the daily maximum. The table also shows the proportion of particulate load less than 7.0 μ. Despite the increasing level of particulates towards the industrial core, there is little change in the proportion of particulate matter less than 7.0 μ.

## Methods

### *Design of Study*

Hamilton, with a population of approximately 300,000, is a city situated at the western end of Lake Ontario. The dominant geographic feature is an escarpment of approximately 100 m high that runs from east to west, effectively dividing the city into a lower section and a mountain section. The city is industrial, with the heavy industrial core, located in the northeast section of the city, being the dominant producer of particulate and $SO_2$ emissions, although there is a secondary $SO_2$ area source in the commercial section located in the western part of the city. Prevailing winds are from the southwest.

Initial air quality monitoring during the pilot study had indicated the presence of substantial gradients for both particulates and $SO_2$, with the mountain section having lower levels than the lower section of the city. On this basis and on the knowledge of prevailing winds, we divided the city into 4 quadrants (figure 1) for the purpose of selection of the sample to be studied. The sampling frame was all public elementary schools within the city of Hamilton. Sample size considerations dictated that at least 800 children would be required within each quadrant. A difference of 5 to 7% in the mean of a particular pulmonary function variable was felt to be necessary for biologic significance. One of the principal outcomes of interest was the measurement of air flow, especially at low lung volumes. Estimates of the mean and standard deviation of these variables were obtained from our pilot study (16) ($FEV_1$: mean, 1.79 L; SD, 0.36; $MEF_{75}$: mean, 1.09 L/s; SD, 0.44). The first criterion employed in sample size determination was that there should be only a 10% chance of missing a biologic difference (Beta error = 0.1). A second criterion was that a difference was considered to exist between the 2 samples if the appropriate statistical test showed that the observed difference had only a 5% chance of occurring in the absence of any real difference (Alpha error = 0.05). Within each of these quadrants, schools were randomly selected until at least 800 children from Grades 2, 3, and 4 during the initial school year had been included. The only children excluded were those older than 10 yr of age by the end of 1978. All children in the required grades from the final school selected in each quadrant were chosen. The children included in the first year of testing made up the initial cohort.

After more detailed air quality monitoring during the first year of the study, it was realized that the area of highest exposure (i.e., TSP annual geometric mean > 60 $\mu g/m^3$) was underrepresented, despite the initial stratification by quadrants in the original design. For this reason, the 3 remaining schools in this area were added, with all children within the required age interval being included.

In addition, in the second year, all children in this same age interval as the initial cohort who moved into a school of study were included in the study. During the third year, no new children were added.

The questionnaire used in the study was one that we had employed in the pilot study. It was developed from a questionnaire used in a similar study in the European Economic Community. The questionnaire covered several aspects of the child's respiratory history, family smoking and respiratory profile, certain aspects of the child's medical background, and information relating to the quality of the dwelling and socioeconomic circumstances of the family. There were differences between our questionnaire and that developed by the American Thoracic Society (17). In our questionnaire, a distinction was made between morning cough and cough during the day or night, the respondent being asked if the child usually coughed in the morning or during the day or night, respectively. Sputum production was not asked about. The question on wheezing inquired if the chest ever sounded wheezy or whistling. In addition, a question about asthmatic attacks in the previous 12 months was included. Two questions related to acute respiratory illness were included. The first asked about a period of cough and phlegm lasting for 3 wk or more and the second about any chest illness keeping the child home for a week or more. (A detailed questionnaire is available from the writers.) In Year 2, questions about early childhood illnesses were added that were derived from the questionnaire designed by the American Thoracic Society (17). Our questionnaire was administered in the home by a trained interviewer to the mother or female guardian, or in her absence, to the father or male guardian. The questionnaire was administered in each of the 3 yr of the study prior to the performance of pulmonary function testing.

Pulmonary function testing was performed at the child's school. Four types of pulmonary function tests were performed: forced expired maneuvers ($FEV_1$, FVC, $MEF_{50}$, $MEF_{75}$, and MET), spirometry (a slow vital capacity (VC) following quiet breathing) (VC, ERV), single-breath nitrogen washout (CV/VC, $N_2$ difference) and multiple-breath

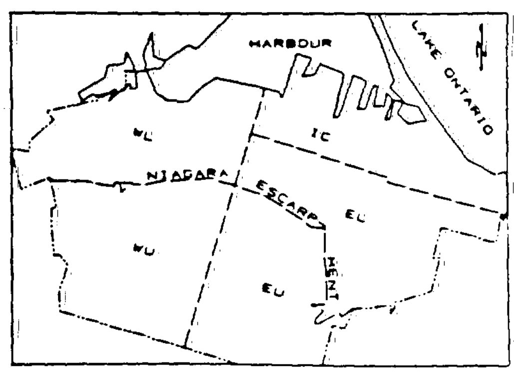


Fig 1. Outline map of Hamilton, Ontario, showing the 4 quadrants chosen in the original design, and the industrial core (IC) (WU = west upper; EU = east upper; WL = west lower; EL = east lower).

nitrogen washout (FRC). The additional use of the single-breath nitrogen washout was justified by the study of Becklake and coworkers (18), who showed an increase in closing volume in children exposed to a high particulate/$SO_2$ environment.

Air quality was measured by a comprehensive particulate and $SO_2$ network. There were 27 monitored sites for TSP using hi-vol samplers, with 9 additional hi-vol samplers with Andersen 4-stage cascade impactors for the measurement of mass median diameter. In addition, there were 16 sites for $SO_2$ monitored in groups of 8, using Beckman 906A monitors (Beckman Instruments, Fullerton, CA), for 6-wk periods in rotation. These sites were distributed throughout the city. Details of air quality monitoring will be contained in a subsequent report.

*Protocol*

In the questionnaire survey, interviewers were randomly assigned to eligible children at each school to be visited, thus ensuring that several interviewers would be assigned to each school. In addition, interviewers were rotated to schools in different parts of the city. The parents had been informed in advance by letter to expect a phone call from the interviewer. The letter also described the purpose of the study as being the investigation of the child's respiratory health. No mention was made of air pollution. Each interviewer telephoned the parent or guardian to arrange for an appointment for questionnaire administration. There was provision for 3 call-backs, if no contact was established initially, before no further attempt at interviewing was made. At the time of contact, the interviewer was able to screen out those children who were older than 10 yr of age in the first year of testing. If the parent consented to the interview, they were then visited by the interviewer. The percentage of those eligible, for whom an interview was not obtained, including those with whom no contact could be established, ranged from 4.6% in Year 1 to 3.3% in Year 3 (table 2). No further attempt was made to follow these. Interpreters were used as necessary, but were required for less than 1% of the parents. At the end of the interview, the pulmonary function test was explained to the parent or guardian, and written consent for the test was obtained at that time. The completed questionnaire was then returned for coding, keypunching, and data storage at the Computation Services Unit at the Health Sciences Centre, McMaster University.

Pulmonary function testing was performed, throughout the school year, within 4 wk of the completion of the interview. Two teams of pulmonary function technicians were assigned alternately to a school in the upper and in the lower part of the city. The testing routine was explained initially to all the students at an assemply and explained further to each child at the time of his or her testing. A questionnaire about smoking habits was also administered to the child at the time of testing in the third year of the study. Pulmonary function testing was performed using the Hewlett-Packard 47804A Pulmonary Calculator System (Hewlett-Packard, Waltham, MA). In this system, flow is measured by a pneumotachygraph, and volume is computed internally by integration with time. Calibration of the 2 systems used was performed twice daily with a 2-L syringe. Correction for ambient temperature and pressure was performed internally by the computer system by entering the appropriate values. After measurement of height and weight, the child first performed a multiple-breath nitrogen washout. This was followed by at least 3 forced expired maneuvers. For acceptance, the 2 largest FVC values had to be within 5% of each other. All measurements were taken from the maneuver with the greatest sum of FVC and $FEV_1$. Spirometry was then performed. If the VC obtained was less than the FVC by more than 10%, the spirometry was repeated until the estimate was within 10%. However, if the VC was greater than the FVC by more than 10%, then the forced expired maneuver was repeated until the FVC estimate was within 10% of VC. Finally, at least 2 single-breath nitrogen washouts were performed in which the expired nitrogen concentration was continuously plotted against VC. The method used was that of Mansell and associates (19), but without the additional dead space. For acceptance of the single-breath nitrogen washout test, the VC had to be within 10% of the largest previous VC from spirometry. If both single-breath maneuvers were acceptable, then the closing volume from the maneuver with the greater VC was taken for analysis. The presence of an upper or lower respiratory infection was noted by the technician at the time of the test. However, the test was always performed, the infection data to be used at the time of analysis to estimate the effect of the infection on pulmonary function. The testing followed the same sequence in Years 2 and 3, except that in Year 3, the single-breath nitrogen washout was omitted because of poor reproducibility (see DISCUSSION). The child was not necessarily tested with the same system nor by the same technician, but comparison of results from the 2 teams was performed at regular intervals to identify any systematic differences.

All measurements of flow and of volume were computed internally, with output being recorded by an on-line printer. Closing volume, however, was computed by inspection of the single-breath nitrogen washout curve, and was taken at that point of inflection of the nitrogen washout curve from a line drawn through phase 3 of the curve (19). These results were then returned for coding, keypunching, and data storage in a manner similar to the questionnaire data.

The quality control of the data gathered was performed in several ways. For both the questionnaire and the pulmonary function coding, a random 5% sample of the data was recoded by a second coder. The reliability of the questionnaire data was estimated by the random selection of 4 interviewers after each pair of schools was completed. For each interviewer, 2 interviews were randomly chosen, and within those interviews, 2 questions were randomly selected. The appropriate respondent was then phoned and the questions were asked again. Apart from estimating the reliability of the answers, this procedure also verified that the original interview had indeed taken place. Interinterviewer variation or bias was estimated by comparing the response rates to certain questions obtained by each interviewer. These data were then examined to see if any differences between interviewers might be greater than that caused by chance alone. When such a difference was found, interviewing technique was reviewed to ensure consistency of technique. In no case was it necessary to change any of the interviewing staff because of poor reliability.

The reliability of the pulmonary function testing was estimated by the retesting of 8 children in each school, 2 children randomly chosen from each age group. All data from pulmonary function testing were passed through a range checking program after data storage, the range being 4 standard deviations centered at the mean, these interval estimates of parameters being derived from the original pilot study. Finally, we were interested in determining any systematic differences between the 2 pulmonary function testing teams. The presence of any differences was estimated by parallel line regression analysis for 4 of the variables measured (FVC, $MEF_{75}$, MET, and CV/VC). This technique used regression analysis to fit a regression line separately to the data collected by each team; if the linear relationship was the appropriate model, then the hypothesis that the 2 lines were parallel was tested. If this hypothesis was not rejected, then the hypothesis that the intercepts were the same was tested. If the second hypothesis was

TABLE 2

CONSENT AND TESTING RATE FOR SAMPLE

| | Year 1 | Year 2 | Year 3 |
|---|---|---|---|
| Eligible for interview | 3,505 | 3,727 | 3,168 |
| Interviews completed | 3,345 | 3,588 | 3,065 |
| Interview completion rate, % | 95.4 | 96.3 | 96.7 |
| Consents given for testing | 3,329 | 3,573 | 3,055 |
| Consent rate, % | 95.0 | 95.9 | 96.4 |
| Number tested | 3,131 | 3,439 | 2,949 |
| Testing completion rate, % | 89.3 | 92.3 | 93.1 |

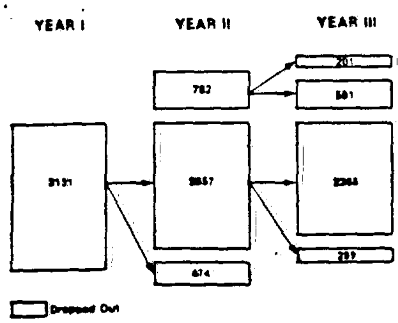


Fig. 2. Maintenance of cohort size, showing numbers lost by attrition and Industrial Core group added during Year 2.

TABLE 3

CHARACTERISTICS OF SAMPLE TESTED

| | Year 1 | | Year 2 | | Year 3 | |
|---|---|---|---|---|---|---|
| | (n) | (%) | (n) | (%) | (n) | (%) |
| Male | 1,611 | 51.5 | 1,769 | 51.4 | 1,513 | 51.3 |
| Female | 1,520 | | 1,670 | | 1,436 | |
| Caucasian | 2,876 | 91.9 | 3,161 | 91.9 | 2,723 | 92.3 |
| Non-Caucasian | 255 | | 278 | | 226 | |
| Total | 3,131 | | 3,439 | | 2,949 | |

TABLE 4

PREVALENCE OF DOMESTIC FACTORS BY AREA OF CITY: YEAR 2*

| | WU | EU | WL | EL | IC |
|---|---|---|---|---|---|
| Number | 829 | 878 | 741 | 863 | 242 |
| Mother smoke | 37.3 | 42.5 | 42.2 | 48.2 | 60.1 |
| Father smoke | 38.3 | 43.4 | 43.3 | 50.2 | 61.3 |
| Mother cough | 15.7 | 15.0 | 17.8 | 17.5 | 28.5 |
| Father cough | 22.1 | 26.4 | 26.1 | 25.6 | 40.4 |
| Gas cooking | 8.3 | 8.3 | 29.7 | 15.6 | 43.4 |
| Share room with 2 or more | 2.3 | 3.6 | 7.3 | 7.0 | 8.8 |
| Income less than $10k/yr | 15.8 | 11.3 | 20.7 | 15.6 | 25.9 |
| Less than 2 yr at present address | 22.4 | 19.0 | 28.2 | 25.6 | 34.4 |

For definition of abbreviations, see table 1.
* Values are percentages. Data missing on 36 subjects.

not rejected then it was concluded that the regression lines for the 2 teams were coincident (20).

A final quality control measure was an examination of the proportion of missing values for each variable for each team, as an indicator of systematic differences between the 2 teams. The analysis and the results of these quality control measures will be described in detail in a separate report. However, the reliability of the questionnaire and pulmonary function data, and the success rates of pulmonary function testing, are described in this report.

Statistical analyses were performed by subprograms in the Statistical Package for the Social Sciences (21). The difference between sample means was tested for significance by subprogram *t* test for paired samples. Pearson's product-moment correlation coefficient, as a measure of association of 2 independent variables, was computed by subprogram scattergram. Hypothesis tests were all two-tailed.

## Results

*Characteristics of Cohort*

The number who were eligible for testing in each year of the study is shown in table 2. To be eligible, the child could not have attained his or her eleventh birthday before December 31, 1978. This table also shows the interview completion rate obtained in each year. The rate, which was above 95% for each year, is considered acceptable. In addition, the percentage giving consent for the pulmonary function testing was virtually identical to that giving consent for interview. There was, however, a degree of attrition after consent was given for pulmonary function testing, before the test was performed. The major reason for this was the child having moved from a testing school into a nontesting school during the time between consent and testing. This attrition was less in Years 2 and 3.

An important feature of the study was the ability to follow the initial cohort into the second and third years of the study. The particular importance of this is the ability to measure changes in pulmonary function variables as the child grows. It is possible that the rate of change of a particular pulmonary function variable might be a more sensitive outcome measure than the use of a single point estimate. The number of children with pulmonary function testing in Year 1 who were tested in Years 2 and 3 (approximately 75% of the original cohort) is shown in figure 2. The figure also shows the number of children added in Year 2 and how many of these were followed into Year 3. The characteristics of the children at the time of pulmonary function

TABLE 5

PREVALENCE OF SMOKING*

| | Age (yr) | | | | | | |
|---|---|---|---|---|---|---|---|
| | 8 | 9 | 10 | 11 | 12 | 13 | Total |
| Any history of smoking† | | | | | | | |
| Yes | 0 (0) | 57 (11.8) | 175 (18.1) | 250 (28.3) | 188 (37.8) | 37 (50.0) | 707 (24.3) |
| No | 3 | 425 | 791 | 634 | 310 | 37 | 2,200 |
| Total | 3 | 482 | 966 | 884 | 498 | 74 | 2,907 |
| Smoking in last 4 wk‡ | | | | | | | |
| Yes | | 2 (3.6) | 28 (16.4) | 41 (17.0) | 56 (30.8) | 12 (32.4) | 139 (20.3) |
| No | | 53 | 143 | 200 | 126 | 25 | 547 |
| Total | | 55 | 171 | 241 | 182 | 37 | 686 |

* Values are frequency with percentages in parentheses.
† Missing observations, 158.
‡ Missing observations, 21.

TABLE 6

REPEATABILITY OF RESPIRATORY SYMPTOM QUESTIONS

| Question | Raw Agreement | Chance-Corrected Agreement (Kappa) |
|---|---|---|
| Cough in morning | 0.92 | 0* |
| Cough during day or night | 0.80 | 0* |
| Chest wheezy or whistling | 0.80 | 0.53 |
| Asthma in previous 12 months | 0.96 | 0.76 |
| Cold goes to chest usually | 1.0 | 1.0 |
| Cough and phlegm for 3 wk in previous 12 months | 0.95 | 0* |
| Absence from school for 1 wk or more in previous 12 months | 1.0 | 1.0 |

* In each case, one marginal was zero, making Kappa an unreliable estimate of chance-corrected agreement.

testing in each of the 3 yr are shown in table 3. There is a slight excess of males over females in each year, and the predominant Caucasian ethnic characteristic of the sample is to be noted.

Previous studies have shown that certain factors other than outdoor air quality can be related to the incidence or prevalence of childhood respiratory disease (7, 10, 13). The distribution of these factors in each of the 4 original quadrants, and also in the additional group of schools in the industrial core that were added in Year 2, are shown in table 4. In this table, a smoker is one who smokes 1 or more cigarettes or cigars per day. The percentage with cough includes those with a positive answer to either of the questions: "Do you usually cough in the morning?" or "Do you usually cough during the day or night?" To simplify the presentation, only the results from Year 2 are shown. However, those from Years 1 and 3 are similar. The prevalence of these factors varied across the city and was highest in the industrial area, where the level of TSP was also the highest (table 1). A further, potentially confounding covariable was the prevalence of smoking by the children themselves. Because the age interval in the first year was between 7 and 10 yr of age, we did not expect to find many smokers. However, by the third year of the study, it might be expected that some of the older children would have commenced regular smoking. We therefore administered a smoking questionnaire to the children at the time of pulmonary function testing. The number of children in each age group who stated that they had smoked at least 1 cigarette in the last 4 wk is shown in table 5.

### *Quality Control*

The repeatability of the respiratory symptom questions is shown in table 6, which details the agreement statistics for each of these questions, both in terms of raw agreement and of chance-corrected agreement (Kappa). In certain cases, Kappa was an unreliable estimate of chance-corrected agreement, because one marginal of the 2 × 2 table from which the Kappa was to be computed was zero. Kappa ranged from a substantial level of 0.56 to an excellent level of 1.0. The percentage of missing values by team for variables derived from the 4 pulmonary function maneuvers is shown in table 7. The values are shown for Year 1. The commonest reason for a pulmonary function value to be missing was that the child could not meet the required criteria for test acceptance. These results, therefore, give a comparison of ability of the 2 teams in obtaining successful tests for each test in each age group. The repeatabilities of the lung function measurements in Years 1 and 2 of the study are shown in tables 8 and 9. There were small but significant differences for several of the measurements (FVC, $MEF_{50}$, $MEF_{75}$, MET, and VC) in Year 1 and to a larger extent in Year 2. The results for Year 3 are not displayed for sake of brevity, but they showed no significant differences. The product-moment correlation coefficients for certain of these variables are shown in table 10 for Year 1. These range from 0.97 for FVC to 0.14 for CV/VC. The reproducibility of these tests might have been affected by the presence of a respiratory infection during either the ini-

TABLE 7

PERCENTAGE OF MISSING VALUES BY TEAM: YEAR 1

| | | Age (yr) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Variable | Team | 6 | 7 | 8 | 9 | 10 | 11 | Total |
| FVC | A | 0.0 | 1.0 | 0.4 | 2.1 | 0.3 | 2.6 | 1.0 |
| | B | 0.0 | 3.3 | 1.6 | 1.3 | 0.9 | 3.4 | 1.8 |
| VC | A | 33.3 | 12.5 | 5.1 | 7.5 | 1.0 | 0.0 | 6.4 |
| | B | 33.3 | 11.5 | 5.4 | 2.4 | 1.8 | 3.4 | 5.1 |
| FRC | A | 16.7 | 5.8 | 3.9 | 4.8 | 1.0 | 0.0 | 3.9 |
| | B | 16.7 | 10.4 | 5.0 | 1.5 | 1.3 | 3.4 | 4.4 |
| CV | A | 66.7 | 49.0 | 28.6 | 23.8 | 12.6 | 5.1 | 27.7 |
| | B | 33.3 | 37.4 | 24.2 | 14.3 | 9.0 | 20.7 | 21.2 |
| $N_2$ difference | A | 66.7 | 49.3 | 28.8 | 23.8 | 12.6 | 5.1 | 27.9 |
| | B | 33.3 | 38.5 | 24.2 | 14.0 | 9.0 | 20.7 | 21.3 |
| Children tested, n | A | 6 | 304 | 532 | 480 | 286 | 39 | 1,647 |
| | B | 6 | 270 | 501 | 456 | 223 | 29 | 1,485 |

*Definition of abbreviations:* CV = closing volume; $N_2$ difference = increase in expired nitrogen concentration during phase III of single-breath nitrogen washout.

TABLE 8

REPEATABILITY OF LUNG FUNCTION MEASUREMENTS: YEAR 1

| | | Initial | | Repeat | | | |
|---|---|---|---|---|---|---|---|
| Variable | n | Mean | SD | Mean | SD | t Value | p Value (2-tailed) |
| FVC | 216 | 2.04 | 0.41 | 2.07 | 0.41 | −3.96 | < 0.001 |
| $FEV_1$ | 216 | 1.67 | 0.31 | 1.66 | 0.31 | 1.33 | 0.190 |
| $MEF_{50}$ | 215 | 2.33 | 0.62 | 2.14 | 0.59 | 3.57 | < 0.001 |
| $MEF_{75}$ | 211 | 0.99 | 0.36 | 0.94 | 0.32 | 3.45 | 0.001 |
| MET | 215 | 0.57 | 0.17 | 0.59 | 0.16 | −3.13 | 0.002 |
| VC | 220 | 2.05 | 0.41 | 2.08 | 0.40 | −3.30 | 0.001 |
| FRC | 210 | 1.19 | 0.31 | 1.19 | 0.29 | 0.13 | 0.895 |
| CV/VC | 166 | 0.134 | 0.09 | 0.12 | 0.078 | 1.42 | 0.158 |
| $N_2$diff | 160 | 1.04 | 0.66 | 1.03 | 0.52 | 0.13 | 0.900 |

*Definition of abbreviations:* MET = midexpiratory time in seconds. For other definitions, see table 7.

TABLE 9
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS: YEAR 2

| | | Initial | | Repeat | | | |
|---|---|---|---|---|---|---|---|
| Variable | n | Mean | SD | Mean | SD | t Value | p Value (2-tailed) |
| FVC | 256 | 2.37 | 0.47 | 2.35 | 0.51 | 2.24 | 0.026 |
| $FEV_1$ | 256 | 1.91 | 0.36 | 1.88 | 0.39 | 2.66 | 0.008 |
| $MEF_{50}$ | 254 | 2.46 | 0.63 | 2.39 | 0.66 | 2.64 | 0.009 |
| $MEF_{75}$ | 254 | 1.05 | 0.34 | 1.03 | 0.35 | 1.49 | 0.138 |
| MET | 256 | 0.59 | 0.16 | 0.60 | 0.19 | −1.79 | 0.75 |
| VC | 255 | 2.39 | 0.47 | 2.36 | 0.49 | 2.37 | 0.019 |
| FRC | 253 | 1.32 | 0.33 | 1.31 | 0.34 | 0.37 | 0.713 |
| CV/VC | 226 | 0.12 | 0.08 | 0.12 | 0.09 | −0.13 | 0.897 |
| $N_2$diff | 226 | 0.88 | 0.50 | 0.85 | 0.44 | 1.35 | 0.178 |

For definition of abbreviations, see tables 7 and 8.

tial or the repeat test. The repeatabilities of the lung function measurements were therefore reanalyzed, omitting from the analysis any test during which the presence of an upper or lower respiratory infection had been recorded. The results from this analysis are shown in table 11. Comparison with table 9 does not indicate that the reproducibility of the test was improved by the exclusion of current respiratory infections. In addition, for no variable was the product-moment correlation coefficient changed by the exclusion of respiratory infections.

### Discussion

This report outlines the background to the study that has been undertaken, the design of this study, and the methods that were used, and it describes the sample that was studied, both in terms of its characteristics and also in terms of important covariables. The design of the study was innovative in selecting schools within each of 4 quadrants of the city in expectation that these areas would show different levels of air quality. However, the area of the city with TSP levels greater than 60 $\mu g/m^3$ annual geometric mean was underrepresented when the air quality results from the first year were analyzed. This required the addition of 3 schools in the industrial core in the second year to achieve a gradient of air quality that one might expect to show an effect on the child's respiratory health. Financial constraints often dictate that air quality monitoring is done at the same time as the measurements of respiratory disease outcomes in children or in adults. However, without detailed prior information about the distribution of air quality gradients, modification of the design may be required during the course of the study, with the increased difficulty this might give in the analysis of the results. Random selection of schools within each quadrant was performed for this health study in the first year but not with the additional schools in the second year, because all the schools in the industrial core (that is, the area of highest particulate levels) were chosen for inclusion in the study.

The cooperation obtained from the Board of Education for the City of Hamilton and the parents of the children was excellent. We feel that the response rate in excess of 95% obtained in each year enables us to extrapolate any conclusions from the sample chosen to the total population of children at risk.

It was not surprising to find that the distribution of covariables, which might influence the child's respiratory health, was not uniform across the city. In the examination of the relationship between levels of air pollutants and respiratory health, it is very important that any confounding effect of covariables be distinguished from the effect of air pollution itself. We have shown that the industrial area, which has the highest level of TSP, has also the highest prevalence of domestic smoking, parental respiratory symptoms, and gas cooking (22).

A further important consideration in the study of the effect of air quality on respiratory health is the previous mobility of the sample being studied. As table 4 shows, the proportion of children who had lived at their present address for less than 2 yr varied from 34.4% in the industrial core to 19.0% on the eastern part of the mountain. This difference would also have to be taken into account in any analysis of these results.

Cigarette smoking by the children themselves also becomes important in this particular age group as it can lead to respiratory disease. Tager and coworkers (23) showed that children's smoking habits must be taken into account when looking at any putative effect of parental smoking. Direct validation of the estimates of smoking obtained from our smoking questionnaire was not performed. However, the percentage of children admitting to smoking in the previous 4 wk does increase in the expected direction with increasing age. In addition, these data are comparable to those obtained by Brown and colleagues (24) in their survey of smoking habits in Canadian school children. We are therefore confident that these results do reflect the smoking habits of the children. However, the rate of 4.8% who had smoked in the previous 4 wk is unlikely to affect the interpretation of the results.

TABLE 10
PRODUCT-MOMENT CORRELATION COEFFICIENT OF INITIAL AND REPEAT ESTIMATES OF PULMONARY FUNCTION VARIABLES

| | Year 1 | Year 2 |
|---|---|---|
| FVC | 0.97 | 0.86 |
| $FEV_1$ | 0.94 | 0.83 |
| $MEF_{50}$ | 0.78 | 0.74 |
| MET | 0.72 | 0.81 |
| RV | 0.40 | 0.43 |
| CV/VC | 0.14 | 0.03 |

TABLE 11
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS
RESPIRATORY INFECTIONS EXCLUDED: YEAR 1

| | | Initial | | Repeat | | | |
|---|---|---|---|---|---|---|---|
| Variable | n | Mean | SD | Mean | SD | t Value | p Value (2-tailed) |
| FVC | 159 | 2.02 | 0.41 | 2.04 | 0.41 | −3.47 | < 0.001 |
| $FEV_1$ | 159 | 1.66 | 0.30 | 1.64 | 0.30 | 0.97 | 0.37 |
| $MEF_{50}$ | 158 | 2.26 | 0.61 | 2.15 | 0.58 | 3.26 | 0.001 |
| $MEF_{75}$ | 158 | 1.00 | 0.34 | 0.94 | 0.32 | 2.99 | 0.003 |
| MET | 158 | 0.56 | 0.17 | 0.58 | 0.16 | −2.93 | 0.004 |
| VC | 162 | 2.03 | 0.40 | 2.05 | 0.40 | −2.55 | 0.012 |
| FRC | 157 | 1.17 | 0.32 | 1.17 | 0.29 | −0.31 | 0.76 |
| CV/VC | 123 | 0.14 | 0.08 | 0.13 | 0.08 | 1.33 | 0.19 |
| $N_2$ diff | 120 | 1.01 | 0.59 | 1.06 | 0.50 | −0.13 | 0.90 |

For definition of abbreviations, see tables 7 and 8.

The results of a number of quality control procedures were part of the study. The repeatability of the respiratory symptom questions was estimated only when those particular questions were asked from the randomly chosen questionnaires. We thought it important to compute chance-corrected agreement (Kappa), because the raw agreement, when the prevalence of a particular symptom is low, may give a false impression of good agreement, when in fact most of the agreement is due to chance alone. For 3 cases, Kappa could not be computed. On the other hand, by the criterion of Landis and Koch (25), agreement was substantial or better for the questions on asthma, colds to chest, and absence from school for more than 1 wk with a chest illness. It was only slightly less than substantial for the question on wheezing or whistling in the chest.

The ability of young children to perform pulmonary function maneuvers is shown in table 7. The forced expired maneuver was the one most successfully performed. In the older age groups, slow spirometry and the multiple-breath nitrogen washout were equally well performed. In contrast, the single-breath nitrogen washout had a failure rate in excess of 20%. This lack of success for this particular test did not improve in Year 2 and it has been our experience that the single-breath nitrogen washout test is a difficult maneuver to employ in large scale epidemiologic monitoring in children.

In tables 8 and 9, it can be seen that in Years 1 and 2 there were small but significant differences between the initial and repeat estimates of a number of the pulmonary function variables that were not due to the presence of a respiratory infection. The differences were not found to be significant, however, in Year 3. No significant differences were found between the initial and repeat estimates for the variables derived from the multiple- and single-breath nitrogen washout maneuvers. However, for these variables, the coefficient of variation was much greater than for the variables derived from the forced expired maneuver, and therefore the analysis was less powerful in being able to demonstrate a difference if one really existed. An additional measure of association, the correlation coefficient, was high for the variables ($FEV_1$ and FVC) derived from the forced expired maneuver, but was much less for those variables derived from the single-breath nitrogen washout. This low correlation reduces considerably the usefulness of the single-breath nitrogen washout test because the amount of random variation may well obscure any true difference between samples.

In conclusion, we have described the design and execution of a study of the effects of environmental factors on the respiratory health of children within a single city. The random selection and high response rate have ensured that the sample is characteristic of the population of interest in the city. The accurate estimation of pollution exposure has required a more comprehensive network of air quality monitors than would normally be employed in a single city. The nonuniform distribution within the city of covariables, such as parental smoking and cough, has implications for the detection of the effects of suspended particulates and $SO_2$, especially when those effects are likely to be small at current levels of these pollutants. If present, these effects are only likely to be detected with samples as large as the one that we have studied.

Pulmonary function testing, even in the youngest of children, had a high rate of success with the exception of the single-breath nitrogen washout. We were disappointed with the lower rate of success of this test, its greater degree of variability, and its lack of reproducibility. For these reasons, it was omitted from the Year 3 testing; we feel that its place in large scale epidemiologic testing has not been justified.

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